**Remarks:**

## Status of Claims

Claims 1, 3, 5-8, 10, 12-13, 15-18, 20-21, 23-25, 45, and 49-50 are pending. Claims 9, 26-43, and 46-48 have been canceled as being directed to non-elected species. Claims 1, 5, 6-8, 10, 12-13, 5-16, 18, 20-21, 23-24, and 45 have been amended. Claims 2, 4, 11, 14, 19, 22, and 44 have been canceled. Claims 49 and 50 are new.

## Claim Objections

The Office objected to claims 4-6, 13-15, and 21-23 for reciting a non-elected invention and objected to claim 44 for reciting non-elected species. Applicant believe that these objections have been addressed by the present claim amendments and the objection has been overcome.

## Priority

The Office Action states that the provisional applications, 60/416,719 and 60/416,718, filed on 10/07/2002, fail to provide adequate support or enablement as required by 35 U.S.C. 112. Thus, the Office Action states that the instantly claimed invention gets the priority filing date of the 60/434,116 provisional application filed on 12/16/2002.

Applicants respectfully disagree with this determination of priority date. As the amended claims recite, the instant invention comprises methods of inhibiting gastrointestinal motility, inhibiting gastric emptying, and inhibiting intestinal transit comprising administering a polypeptide comprising the amino acid sequence of amino acid residues 28 to 108 of SEQ ID NO:2. Support for these claims can be found in the applications filed on 10/07/2002 in Example 4, wherein the specification teaches:

> "This reduction in transit time may be the result of a massive muscle contraction at such high doses. Zven1 may well increase motility in vivo at low doses, as observed in an organ bath, and inhibit motility at high doses. "

In addition, the earliest-filed specifications teach in vivo models to measure inhibition of diarrhea, such as those described on page 53 of the provisional applications. Thus, there is clear support and enablement for the instant invention as of the 10/07/2002 filing date. Applicants respectfully request this priority date be accorded to the instant invention.

## Claim Rejections – 35 USC § 112, first paragraph

Claims 1-8, 10-25 and 44-45 were rejected under 35 USC § 112, first paragraph, because the Office alleges that specification, while being enabling for stimulating gastrointestinal contractility, does not reasonably provide enablement for inhibiting gastrointestinal contractility. The Office Action states that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The Office relies on factors discussed in Ex parte Forman such as, the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quality of experimentation needed, to conclude that the Office believes that the instant disclosure fails to meet the enablement requirement.

### The Nature of Invention:

The presently claimed invention is drawn to methods of inhibiting gastrointestinal motility, inhibiting gastric emptying, and inhibiting intestinal transit comprising administering a polypeptide comprising the amino acid sequence of amino acid residues 28 to 108 of SEQ ID NO:2.

### The state of the prior art and the predictability or lack thereof in the art:

The Office Action states that it is known in the art an intestinal contraction can be stimulated or inhibited to modulate food processing in the gut. Additionally, the Office Action states that Zhou et al teach that a polypeptide named Prokineticin-2, which is identical to the polypeptide of SEQ ID NO: 2 of the present application, can stimulate gastrointestinal contractility. The Office Action also states that Zhou et al do not disclose that the peptide can inhibit gastrointestinal contractility. Thus, the Office concludes that it would not be predictable to use the instantly claimed polypeptide to inhibit gastrointestinal contractility.

Applicants believe that the Office erred when it concluded that the instant specification does not teach that administering the claimed polypeptide inhibits gastrointestinal contractility, and that one skilled in the art would not be able to practice the claimed invention. This point has already been addressed in the discussion of priority above, where Applicants have shown that support for the amended claims can be found in the earliest-filed applications: in Example 4 and the in vivo models on page 53 of the provisional applications. Additional teachings can be found in the applications filed on 12/16/2002 in Example 8, which looked at the effects of the claimed polypeptide in an in vivo model of gastric emptying and intestinal transit. The example concludes, "These data suggest that at higher concentrations, zven1 can inhibit gastric emptying and intestinal transport."

**The amount of direction or guidance present and the presence or absence of working examples:**

The Office relies on the incorrect conclusion from the previous section, i.e., that the instant specification does not teach that administering the polypeptide of the claimed invention inhibits gastrointestinal contractility, to further argue that the detailed teachings necessary to enable one skilled in the art to practice the instant invention commensurate with the scope of the claims, are not present in the instant specification.

As addressed above, such teachings are clearly presented in Example 4 (as taught in the applications filed on 10/07/2002) and Example 8 (as taught in the applications filed on 12/16/2002). In addition, the instant specification (filed on 10/07/2003) teaches many supplemental models on pages 70-75. See also Example 21, page 112, lines 18-22:

> "Inhibitory effects of gastric emptying and intestinal transit were observed using higher doses (10-100 ug/kg BW for i.p. dosing; 30 ug/kg BW for i.v. dosing) of BV- and E. coli-Zven1. The inhibitory observations were especially evident when these higher doses of Zven1 were administered i.v. at 1 minute following test meal administration, or when administered i.p. at 10 minutes prior to test meal administration."

Additionally, see Example 22, page 113, lines 11-13:

> "Trends toward inhibition of gastric emptying and intestinal transit were observed using higher doses (> 50 ug/kg i.v. in mice) of Zven1."

Thus, the instant specification clearly provides not only working examples, but additional guidance on the claimed invention.

**The breadth of the claims and the quantity of experimentation needed:**

The Office Action further states that in light of the teachings in the art discussed and because of the lack of sufficient teachings in Applicant's disclosure, the specification is not enabled. The Office suggests that this rejection could be overcome by replacing the claim language of "inhibiting contractility" with language in which transit thought the gastrointestinal tract is inhibited.

Applicant's believe that, in addition to the instant claim amendments, they have pointed the Office to the disclosure in the application to overcome these rejections.

Based on the amendments and arguments presented herein, Applicants believe that this rejection has been overcome. Applicants respectfully request this rejection be withdrawn.

## Claim Rejections – 35 USC § 112, second paragraph

Claims 1, 10, 18 and 44 were rejected under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Office alleges that the phrase "modulating" renders the claim indefinite because it is unclear whether the term "modulation" is increase in gastrointestinal contractility or it is a decrease in gastrointestinal contractility.

Claims 1, 10, and 18 have been amended to recite "inhibition". Claim 44 has been canceled. Applicants respectfully request this rejection be withdrawn.

## Double Patenting – 10/990,246

The Office provisionally rejected claims 1-8, 10-25, and 44-45 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of co-pending Application No. 10/990,246. The Office bases this rejection on the grounds that while the claims of the co-pending 10/990,246 are drawn to "stimulating or treating" rather than "inhibiting", there is no dosage requirement for the instantly "inhibiting" claims and the method steps and peptides recited are exactly the same.

Applicants disagree with this rejection. As the amended claims recite, the instant invention comprises methods of inhibiting gastrointestinal motility, inhibiting gastric emptying, and inhibiting intestinal transit comprising administering a polypeptide comprising the amino acid sequence of amino acid residues 28 to 108 of SEQ ID NO:2. Claims to methods of *inhibiting* gastrointestinal motility, *inhibiting* gastric emptying, and *inhibiting* intestinal transit do not encompass claims to *stimulating* gastrointestinal contractility, *stimulating* gastric emptying, or *stimulating* intestinal transit. Furthermore, since gastroparesis is a disorder in which the stomach takes too long to empty its contents, a method of treating gastroparesis would not entail inhibiting gastrointestinal motility, gastric emptying, and intestinal transit. Applicants respectfully request this rejection be withdrawn.

## Claim Rejections – 35 USC § 102

Claims 1-8, 10-25 and 44-45 were rejected under 35 USC § 102(e) as being inherently anticipated by Zhou et al. (US20020115610A1 Published on 08/22/02, with an effective filing date 11/03/00 of US 60/245,882). The Office states that Zhou et al teach a polypeptide with 100 % identity with SEQ ID NO: 2 of the instant application, and that while Zhou do not explicitly teach that the polypeptide can inhibit GI contractility, the polypeptide and the method steps are the same as those being instantly claimed. Therefore, the Office concludes that the teachings of Zhou et al inherently meet all the limitations of the claimed invention.

Applicants respectfully disagree with the conclusion that methods of inhibiting gastrointestinal motility, inhibiting gastric emptying, and inhibiting intestinal transit comprising administering a polypeptide comprising the amino acid sequence of amino acid residues 28 to 108 of SEQ ID NO:2 is inherent in the teachings of Zhou et al. It is not inherent from Zhou that administering a polypeptide comprising the amino acid sequence of amino acid residues 28 to 108 of SEQ ID NO:2 is inhibitory. From the teachings of the present specification, it is shown that not all dosages of the polypeptide are shown to inhibiting gastrointestinal motility, inhibiting gastric emptying, and inhibiting intestinal transit. Zhou et al, do not show this inhibitory effect. Rather discussion in the Zhou specification relates to use of antagonists, such as antibodies, to inhibit the gastrointestinal contractility effects of the polypeptide. Thus, administering the polypeptide does not necessarily result in inhibition. Furthermore, based on the teachings of Zhou et al, one skilled in the art would not recognize that administration of the polypeptide would result in inhibition. Thus, Applicants respectfully request this rejection be withdrawn.

## Amendment of Inventorship

In addition, prosecution of the present application has resulted in the amendment or cancellation of claims so that fewer than all of the currently named inventors are the actual inventors of the invention being claimed. Applicants request the deletion of Robert R. West, Paul O. Sheppard, Stephen R. Jaspers, Anitra Wolf, Susan D. Holderman, and Chung Chan who are no longer inventors of the invention being claimed. As required, attached is a Request to Correct Inventorship pursuant to 37 C.F.R. §1.48(b) and the processing fee set forth in § 1.17(i).

Reconsideration of the application in view of the above amendments and following remarks is requested. Claims 1, 3, 5-8, 10, 12-13, 15-18, 20-21, 23-25, 45, and 49-50 are now in the case. Claims 9, 26-43, and 46-48 have been canceled as being directed to non-elected species. Claims 1, 5, 6-8, 10, 12-13, 5-16, 18, 20-21, 23-24, and 45 have been amended. Claims 2, 4, 11, 14, 19, 22, and 44 have been canceled. Claims 49 and 50 are new.

Applicant(s) assert(s) that the present amendment adds no new matter.

Applicants reserve the right to prosecute claims to cancelled subject matter in one or more continuing applications.

On the basis of the above amendments and remarks, Applicants believe that each rejection has been addressed and overcome. Reconsideration of the application and its allowance are requested. If for any reason the Examiner feels that a telephone conference would expedite prosecution of the application, the Examiner is invited to telephone the undersigned at (206) 442-6752.

It is believed that no fee is due. However, in the event that a fee is due, please charge any fee or credit any overpayment to Deposit Account No. 26-0290.

Respectfully Submitted,

Deborah A. Sawislak
Deborah A. Sawislak
Registration No. 37,438

Enclosure:
Request to Correct Inventorship pursuant to 37 C.F.R. §1.48(b)

Customer No. 10117
ZymoGenetics, Inc.